Dr. Barie has described a small series of patients with AIDS who underwent percutaneous cholecystostomy for acute cholecystitis, with good results and little associated morbidity. Because of this limited experience, he suggests that this is the "standard of care" at his institution. Percutaneous cholecystostomy has a distinct role in the management of patients for whom the risks of operative intervention and anesthesia are overwhelming. But our institutional experience and an extensive review of the literature suggest that surgery is contraindicated in only the smallest minority of patients with AIDS-related biliary disease. We have demonstrated that cholecystectomy is a safe intervention in this population of patients. Cholecystectomy resolves the pathology by removing the infected organ and provides more lasting benefit. The expected survival after a bout with cholecystitis is measured in years, not weeks or months. For this reason, the likelihood of ultimately having to intervene surgically is high after a temporizing procedure such as cholecystostomy.

There are other reasons to avoid cholecystostomy in patients with AIDS. Longterm, indwelling drains in patients with infectious disease may pose a biohazard, both in the hospital and in the home setting. Definitive cholecystectomy may also help to resolve infection in the remaining portion of the biliary tree. Our experience with a small number of patients who had biliary tree (including gallbladder) overgrowth with either cryptosporidium or cytomegalovirus suggests that once the gallbladder is removed, overgrowth of the biliary tree regresses. I am concerned that such regression in disease may not follow drainage alone.

As our understanding of HIV and AIDS has grown, we have been better able to discern the true role of surgery in the treatment of its complications. The most difficult distinction is in determining what level of therapy is "too" aggressive and what is not aggressive enough. In our experience, cholecystectomy represents the appropriate level of care for patients with HIV/AIDS who have cholecystitis.

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Pancreas Transplantation

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The article entitled ". . .Surgical Risk of Pancreas Transplantation. . ." by Gruessner, Sutherland, and associates in the August issue emphasizes several important points about this complex procedure, which is still viewed as "experimental" by several health care funding agencies, including the Health Care Financing Administration.

The Minnesota group, which initiated the clinical procedure in 1966,[1] has pioneered the evolution of pancreas transplantation for the past 3 decades under the direction of David Sutherland. The question has always been raised whether the procedure, which is associated with considerable morbidity, is worth the potential risk. The authors have presented an honest appraisal of the risk factors together with details, statistics, and results, including the effects of surgical complications on graft success rates and patient survival. Of particular interest, the subgroup of recipients that required relaparotomy (32%) had a 77% 1-year patient survival rate in the pancreas/kidney group compared with an 87% survival rate in the remaining 68% who did not require reoperation. The effect of relaparotomy on 1-year graft survival was more devastating: 32% versus 82%.

In our series of 123 consecutive patients who received cadaveric pancreas transplantation in the last 3 years (all but 17 having simultaneous transplantation with a kidney), one died after multiple reoperations for septic complications. Two others having no relaparotomy died at 4 and 8 months of posttransplant lymphoma and a midbrain stroke, respectively. Our graft success rate (median followup 1.5 years) was 56% in the 41 reoperated patients versus 95% in the 82 patients who did not require relaparotomy. If nine patients with low perfusion/thrombosis requiring graft removal within the first week were excluded from the reoperated group, the graft success rate was 78%.

Although we continue to use bladder drainage in some recipients of pancreas-only to monitor the urinary amylase level as an indicator of rejection, we have increasingly used enteric drainage for all pancreas grafts because of its lower complication rate.[2] Dehydration and acidosis do not occur, eliminating the conversion from bladder to enteric drainage, which has been necessary in nearly 20% of patients at some centers.[3]

Our use of tacrolimus-based immunosuppression without prophylactic antilymphoid induction therapy and rapid tapering of steroids has reduced the incidence of both viral and bacterial infections, while allowing good control of rejection. In recipient selection, it is important to avoid patients with advanced, uncorrectable coronary artery disease. In our opinion, donor exclusion based on an arbitrary age ceiling is unnecessarily restrictive. A decision to use an organ can be made wisely from its gross appearance and texture, the adequacy of the venous efflux of chilled flush solution after benchwork reconstruction, and the quality of the vessels.

Surgical complications associated with pancreas transplantation should not necessarily result in an increased mortality rate or a high incidence of graft loss.

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In Reply

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We appreciate the interest and the insightful comments of Drs. Corry and Starzl regarding our article "The Surgical Risk of Pancreas Transplantation in the Cyclosporine Era: An Overview," published in the *Journal of the American College of Surgeons* in August 1997.[1] Drs. Corry and Starzl of the University of Pittsburgh raised the following issues, all pivotal to successful pancreas transplantation: 1) immunosuppressive therapy, 2) management of pancreas graft exocrine secretions, 3) donor and recipient selection criteria, and 4) the impact of surgical complications on outcome.

1) As stated in its title, our article represents a historic overview of the surgical risk of pancreas transplantation in the cyclosporine era, covering the period from January 1, 1986 through July 31, 1994. Since mid-1994, tacrolimus has been used by many transplant centers (including ours) as the mainstay of immunosuppressive therapy after pancreas transplantation. Drs. Corry and Starzl reported improved patient and graft outcomes in their series when tacrolimus was used. The superiority of tacrolimus-based (over cyclosporine-based) immunosuppression has also been documented in a multicenter analysis.[2] In our historic overview, patients receiving tacrolimus were not included.

Since August 1, 1994, we have used tacrolimus-based immunosuppression for 234 pancreas transplant recipients. As in the Pittsburgh experience, our 1-year patient and graft survival rates (95% and 78%, respectively) have been significantly higher with tacrolimus than with cyclosporine. A total of 51 (22%) patients receiving tacrolimus underwent relaparotomy (compared with 32% in the cyclosporine era, as stated in our article). Similarly, only 23 recipients (10%) of tacrolimus required treatment for intraabdominal infection (compared with 20% in the cyclosporine era, as stated in our article). In the tacrolimus era, not only has the surgical complication rate decreased, but the number of graft losses from rejection has also decreased. These improvements in overall outcome are largely due to tacrolimus, but also reflect the introduction of another new immunosuppressive drug, mycophenolate mofetil; the use of more efficient, yet less toxic, antimicrobial agents; refinements of the transplant procedure itself; better diagnosis of rejection because of more liberal use of biopsies; and better selection of donors and recipients.

Drs. Corry and Starzl suggest that tacrolimus-based immunosuppression allows avoidance of prophylactic anti–T-cell induction therapy after pancreas transplantation. This possibility still needs to be studied prospectively. A multicenter study will begin by the end of this year that will use tacrolimus-based immunosuppression and will compare outcomes with, versus without, anti–T-cell induction therapy.

2) The optimal technique to handle pancreas graft exocrine secretions has been the subject of ongoing discussion since the beginning of pancreas transplantation. Historically, the incidence of technical failure has been greater with enteric (versus bladder) drainage—one of the reasons that bladder drainage has become the most common technique to drain the exocrine secretions. In addition, bladder drainage allows graft exocrine function to be monitored by measuring pancreas enzymes secreted directly into the urine. The disadvantage of bladder drainage is that it can cause metabolic, pancreatic, or urinary complications that may ultimately require takedown of the duodenocystostomy and conversion to enteric drainage.

Enteric drainage will replace bladder drainage only if it can be shown that graft survival is equiva-

lent, both shortterm and longterm. According to the latest update by the International Pancreas Transplant Registry,[3] the 1-year graft survival rate with bladder drainage is 83%; with enteric drainage with Roux-en-Y, 80%; and with enteric drainage without Roux-en-Y, 77% (overall $p < 0.1$). The difference in graft survival is not significant for bladder drainage versus enteric drainage with Roux-en-Y or for enteric drainage with versus without Roux-en-Y. But the difference is significant for bladder drainage versus enteric drainage without Roux-en-Y.[3] These results have been reported only for recipients of simultaneous pancreas-kidney transplants, in whom the kidney graft is considered a surrogate marker of rejection. Because renal markers for rejection cannot be used after solitary pancreas transplantation, we currently recommend against enteric drainage for solitary pancreas grafts.

3) Outcomes after pancreas transplantation are largely influenced by prudent selection of donors and recipients. In a multivariate analysis, we showed previously that the presence of pretransplant cardiac disease (myocardial infarction, bypass, angioplasty) placed pancreas transplant recipients at a higher risk of death with a functioning graft.[4] This finding is in line with Drs. Corry and Starzl's recommendation not to perform transplantation in candidates with advanced, uncorrectable coronary artery disease.

We have recommended against the use of donors $\geq$ 45 years old. We agree that this arbitrary age ceiling is restrictive, but it provides a guideline for smaller transplant centers. Repeated analyses by the International Pancreas Transplant Registry have shown significantly less favorable outcomes with donors $\geq$ 45 years old.[3] Surgeons with experience in pancreas transplantation can and should weigh other factors (besides donor age) in deciding on a particular donor organ, such as its gross appearance and texture. In our own experience, pancreas grafts from donors $\geq$ 45 years old can be transplanted successfully, but results are more consistently good with donors $<$ 45 years of age.

4) In our experience, surgical complications continue to have a negative impact on graft outcomes and hospital costs,[5] despite the use of tacrolimus. In the Pittsburgh series, graft survival was 39% lower for recipients who underwent a relaparotomy after transplantation versus those who did not. In our series, 1-year graft survival in recipients of tacrolimus was 83% without versus 55% with a relaparotomy after transplantation ($p < 0.0001$). Pancreas transplantation remains a procedure that requires meticulous attention to technical detail. Any minor technical error can have catastrophic consequences.

In conclusion, we agree with Drs. Corry and Starzl that tacrolimus has further improved the results of pancreas transplantation. More than 1,000 pancreas transplant procedures are now performed annually in the United States. This procedure has become a well-established treatment option for patients with insulin-dependent type I diabetes mellitus. We hope that, in the near future, Medicare and Medicaid will join the increasing number of insurance providers that cover pancreas transplants.

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